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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,038	07/10/2000	Antonio J. Grillo-Lopez	P1752R1	9334

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Attn Wendy Lee
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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
08/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/613,038	GRILLO-LOPEZ ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 6,8-10,16,22,32-34,37,41,45-60,62 and 63 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 6,8-10,16,22,32-34,37,41,45-60,62,63 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 6/27/07.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant's election of host versus graft in the reply filed on 6/27/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. In view of the papers filed 2/8/07, the inventorship in this nonprovisional application has been changed by the deletion of Mark D. Pescovitz.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The declaration is defective because it includes Timothy Stewart/ Mark D. Pescovitz who are no longer inventors.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of claims 1, 6-16, 22, 28, 32-60 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in the previous Office Action, paragraph 8 is withdrawn in view of the cancellation of claims that have been cancelled and applicants arguments.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The rejection of claims 1, 6, 12-16, 22, 28, 34-39, 43,44 under 35 U.S.C. 102(b) as being anticipated by WO 98/04281 (IDS Ref. No. 31) for the reasons elaborated in the previous Office Action are withdrawn in view of the amended claims and cancellation of claims that have been cancelled.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. The rejection of claims 1, 6-10, 12-16, 22, 28,32, 34-41, 43,44 under 35 U.S.C. 103(a) as being unpatentable over WO 98/04281 (IDS Ref. No. 31) in view of Business Wire (2/24/1998) for the same reasons set forth in the previous Office Action

are withdrawn in view of the cancellation of claims that have been cancelled and the amended claims.

10. The rejection of claims 1,6-10,12-16,22,28,33, 34-39,42-44 under 35 U.S.C. 103(a) as being unpatentable over WO 98/04281 (IDS Ref. No. 31) in view of U.S. Pat. No. 6,498,181 for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claims.

11. Claims 6,8-10,16,22,32,34,37,41,45-60,62,63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meyer et al. (EP 0332865) in view of Anderson et al. (US Patent 5,736,137). Applicants arguments have been considered and deemed not persuasive.

Meyer et al. teach use of antiB cell antibody to treat transplant rejection (see column 2 and column 3, last two paragraphs). Meyer et al. teach that said antibody can be used unconjugated or conjugated to a toxin or radioisotope (see column 3). Meyer et al. teach that said antibody can be antibodies that bind human B cells (see column 3). Meyer et al. do not teach use of antiCD20 antibody or the particular species of antiCD20 antibodies recited in the claims. Anderson et al. teach that treatment with the chimeric antiCD20 antibody C2B8 (alias Rituximab or RITUXAN) can be used to effectively deplete B cells in vivo (see columns 25-28). C2B8 binds the B cell surface antigen CD20. Anderson et al. teach a dose range encompassed by those recited in the claims (see column 8). Anderson et al. also teach B cell depletion using RITUXAN at a variety of dosages (See TABLE 1), wherein said doses are less than 375 mg/ patient. Meyer et al. teach that the anti B cell antibody used can be chimeric and is cytotoxic to B cells (see page 3). The chimeric antiCD20 antibody C2B8 taught by Anderson et al. has both these properties. Anderson et al. also teach the radiolabeled antibody Y2B8 (see column 30).

Humanized and human antibodies binding a desired target, methods of making said antibodies and the advantage of such antibodies were well known in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Meyer et al. teach that antibody against a B cell surface marker can be administered to treat transplant

rejection, while Anderson et al. teach that treatment with the chimeric antiCD20 antibody C2B8 (alias Rituximab) can be used to effectively deplete B cells in vivo at dosages encompassed by those recited in the claims. One of ordinary skill in the art would have been motivated to do the aforementioned because Meyer et al. teach that the anti B cell antibody used can be chimeric and is cytotoxic to B cells, while Anderson et al. teach that C2B8 chimeric antiCD20 antibody effectively depletes B cells when administered in vivo. Anderson et al. teach subcutaneous or intravenous administration of said antibody (see column 7, last paragraph). Anderson et al. teach a dose range encompassed by those recited in the claims (see column 8). A routineer would have increased the second dose of antibody if the first dose of antibody did not provide the required results. The method also includes use of an immunosuppressive agent (OKT3, see page 3, last paragraph).

Regarding applicants comments, claims 45/46 are considered open in scope and therefore equivalent in scope to "comprising". Regarding applicants comments about the agents used in the claimed methods, the claimed methods encompass use of agents in addition to antiCD20 antibody. Regarding the proposed mechanism of action as disclosed by Meyer et al., said mechanism of action is irrelevant to the discussion under consideration because the claimed rejection renders obvious the administration of antiCD20 antibodies to the same patients recited in the claims. Regarding applicants comments about use of Lym-1 or Lym-2 in the method of Meyer, said antibodies are merely used as examples of antibodies that could potentially be used. Meyer clearly teaches that **any cytotoxic antibody which binds B cells** can be used in the method which he discloses (see claims). Regarding applicants comments about "mature B cells", the claims of Meyer teach use of anti B cell antibodies and are not limited to use of antibodies against mature B cells. In view of the disclosure of Anderson et al. of the superior B cell cytotoxicity of the C2B8 antibody (aka rituximab), it would have been obvious to use said antibody in the method of Meyer. Regarding the functional property of the antiCD20 antibody recited in the claim, Meyer discloses use of chimeric antibodies wherein the "constant regions have been altered or replaced with domains which fix complement proteins or elicit target cell destruction by virtue of antibody-dependent cellular cytotoxicity" indicating that the antibody used would lyse B cells and

therefore reduce circulating levels of B cells in humans. Anderson et al. teach that treatment with the chimeric antiCD20 antibody C2B8 (alias Rituximab or RITUXAN) can be used to effectively deplete B cells in vivo (see columns 25-28). C2B8 binds the B cell surface antigen CD20. Regarding applicants comments about agents used in the claimed method, both the claimed method and the prior art encompass use of antiCD20 antibody in connection with another therapeutic agent. The antiCD20 antibody rendered obvious for use in the claimed method is the same as that recited in the claims (aka rituximab). Even to the extent that the rationale for using the antibody may be different in the two methods, the MPEP section 2144 discloses that the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant.

RATIONALE DIFFERENT FROM APPLICANT'S IS PERMISSIBLE
The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied,
500 U.S. 904 (1991) (discussed below). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done" (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. In In re Linter the claimed invention was a laundry composition consisting essentially of a dispersant, cationic fabric softener, sugar, sequestering phosphate, and brightener in specified proportions. The claims were rejected over the combination of a primary reference which taught all

the claim limitations except for the presence of sugar, and secondary references which taught the addition of sugar as a filler or weighting agent in compositions containing cationic fabric softeners. Appellant argued that in the claimed invention, the sugar is responsible for the compatibility of the cationic softener with the other detergent components. The court sustained the rejection, stating "The fact that appellant uses sugar for a different purpose does not alter the conclusion that its use in a prior art composition would be [sic, would have been] prima facie obvious from the purpose disclosed in the references." 173 USPQ at 562. In In re Dillon, applicant claimed a composition comprising a hydrocarbon fuel and a sufficient amount of a tetra-orthoester of a specified formula to reduce the particulate emissions from the combustion of the fuel. The claims were rejected as obvious over a reference which taught hydrocarbon fuel compositions containing tri-orthoesters for dewatering fuels, in combination with a reference teaching the equivalence of tri-orthoesters and tetra-orthoesters as water scavengers in hydraulic (nonhydrocarbon) fluids. The Board affirmed the rejection finding "there was a reasonable expectation' that the tri- and tetra-orthoester fuel compositions would have similar properties based on close structural and chemical similarity' between the tri- and tetra-orthoesters and the fact that both the prior art and Dillon use these compounds as fuel additives'." 919 F.2d at 692, 16 USPQ2d at 1900. The court held "it is not necessary in order to establish a prima facie case of obviousness . . . that there be a suggestion or expectation from the prior art that the claimed [invention] will have the same or a similar utility as one newly discovered by applicant," and concluded that here a prima facie case was established because "[t]he art provided the motivation to make the claimed compositions in the expectation that they would have similar properties." 919 F.2d at 693, 16 USPQ2d at 1901 (emphasis in original). See MPEP § 2145, paragraph II for case law pertaining to the presence of additional advantages or latent properties not recognized in the prior art.

In addition, In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device , and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill".**

The method rendered obvious in the instant rejection uses the same reagents as encompassed by those recited in the claimed invention. Regarding applicants comments about use of Lym-1 or Lym-2 in the method of Meyer, said antibodies are merely used as examples of antibodies that could potentially be used. Meyer clearly teaches that any cytotoxic antibody which binds B cells can be used in the method which he discloses (see claims). Regarding applicants comments about "mature B cells", the claims of Meyer teach use of anti B cell antibodies and are not limited to use of antibodies against mature B cells. In view of the disclosure of Anderson et al. of the superior B cell cytotoxicity of the C2B8 antibody (aka rituximab), it would have been obvious to use said antibody in the method of Meyer. Regarding applicant comments about parameters of the antiCD20 antibody, the antibody is used at a concentration to deplete B cells wherein said concentration would be the same as that recited in the claims when the antibody used was using dosages disclosed in Anderson et al. Meyer discloses use of antibodies against B cells per se and is not limited to use of anti Lym 1 or 2 antibody and that the antibody used should be cytotoxic). In addition, in view of the superior properties of the C2B8 antibody for depleting B cells as per taught by Anderson et al. it would have been obvious to use said antibody in the method of Meyer.

12. Claims 10,33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meyer (EP 0332865) in view of Anderson et al. (US Patent 5,736,137) as applied to claims 6,8-10,16,22,32,34,37,41,45-60,62,63 above, and further in view of U.S. Pat. No. 6,498,181. Applicants arguments have been considered and deemed not persuasive.
The previous rejection renders obvious the claimed invention except for use of ^{131}I-B1. The `181 patent teaches ^{131}I labeled anti-B1 (Bexxar) mAb, raised to the CD-20 antigens that are expressed on the surface of mature B-cells, is one example of a radiolabeled mAb that has seen successful in treating follicular non-Hodgkin's lymphoma in recent clinical trials (see co. 9, lines 19-30 in particular). It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody to human CD20 taught by the `137 publication with the $^{131}$I-B1 antibody as taught by the `181 patent. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because ^{131}I-B1 has

seen successful in vivo in humans. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants arguments regarding Meyer/Anderson are essentially as addressed above. Regarding applicants comments, “281" should be "137" (aka the actual reference cited in the rejection). Regarding applicants comments, use of radiolabeled antibody against antiCD20 was already taught by Anderson et al. (see reference to said antibody in the rejection of paragraph 12 upon which this rejection is based). Therefore a routineer would have substituted a different radiolabeled antiCD20 antibody (^{131}I labeled anti-B1 (Bexxar) mAb) for that antibody disclosed in Anderson et al. In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device , and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill".**

13. Claims 6,22,45,47,49,50,62 are rejected under 35 U.S.C. 102(a) as being anticipated by Perrotta et al. Applicants arguments have been considered and deemed not persuasive.

The claims under consideration encompass a method of blocking an immune response in a human that has not received a graft. Perrotta et al. disclose treat with rituximab (aka the chimeric antiCD20 antibody formerly known as C2B8) via multiple infusions (aka intravenous infusion) at a dosage encompassed by that recited in the claims wherein the antibody would inherently have the properties recited in the claim because it is the same antibody as recited in the claims administered at the same concentration. The patient did not suffer from a malignancy. Rituximab is unconjugated C2B8.

Regarding applicants comment, claim 45 recites blocking "an immune response to an allogeneic graft", thus said claim reads on blocking an "immune response". As per original claim 22/1, the response can be blocked prior to grafting. The claim does not recite that the human has received a graft. It recites that an immune response to an

allogeneic graft is blocked. The potential immune response to the graft exists prior to grafting and is innate.

14. The rejection of claims 1,6-10,13-15,22,32-36,43,45,47-53 under 35 U.S.C. 102(e) as being anticipated by Goldenberg et al. (US 2003/0133930) is withdrawn in view of applicants arguments.

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron, Ph.D./
Primary Examiner, Art Unit 1644